

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>P34780A/CMU/MCM</b>	<b>FOR FURTHER ACTION</b> <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/GB2004/003342</b>	International filing date (day/month/year) <b>30/07/2004</b>	(Earliest) Priority Date (day/month/year) <b>30/07/2003</b>
Applicant <b>THE QUEEN'S UNIVERSITY OF BELFAST</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (See Box II).

3. ☒ Unity of invention is lacking (see Box III).

4. With regard to the title,

- ☐ the text is approved as submitted by the applicant.
- ☒ the text has been established by this Authority to read as follows:

**IN VITRO GENE EXPRESSION ASSAY FOR DETERMINING FLUOROPYRIMIDINE SENSITIVITY IN CHEMOTHERAPY**

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 39.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_
- ☐ as suggested by the applicant.
- ☐ as selected by this Authority, because the applicant failed to suggest a figure.
- ☐ as selected by this Authority, because this figure better characterizes the invention.
- b. ☒ none of the figures is to be published with the abstract.

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International application No.

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**Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of Item 1.b of the first sheet)**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☐ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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International application No.  
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### Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☒ Claims Nos.: 24  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-20 (partially)

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 24

Present claim 24 relates to a chemotherapeutic agents defined by reference to a desirable characteristic or property, namely being identified by the method of any one of claims 11 to 16. The claim covers all chemotherapeutic agents having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for none of such chemotherapeutic agents. In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the claimed scope is impossible. Independent of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define the chemotherapeutic agents by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the claimed scope impossible. Consequently, no search has been carried out for claim 24.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-20 (all partially)

Methods for inducing, enhancing, evaluating the in vitro response of tumour cells from a subject to the presence of a chemotherapeutic agent to predict the response of the tumour cells in vivo to the treatment with the chemotherapeutic agent by determining the expression level of the Raf gene.

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Invention 2: claims 1-20 (all partially)

Methods for inducing, enhancing, evaluating the in vitro response of tumour cells from a subject to the presence of a chemotherapeutic agent to predict the response of the tumour cells in vivo to the treatment with the chemotherapeutic agent by determining the expression level of the K-ras gene.

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Inventions 3 to 30: claims 1-21 (all partially) 22,23 (both complete)

Methods for inducing, enhancing, evaluating the in vitro response of tumour cells from a subject to the presence of a chemotherapeutic agent to predict the response of the tumour cells in vivo to the treatment with the chemotherapeutic agent by determining the expression level of one of the genes listed in claim 1.

(Invention 3 = SLAP gene, ....., Invention 14 = thymosin beta 4, ....., Invention 30 = ribosomal protein L7)

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International Application No  
PCT/GB2004/003342

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C12Q1/68				
According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12Q				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched				
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-internal, BIOSIS, EMBASE, MEDLINE, WPI Data, PAJ, Sequence Search				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	MAXWELL PAMELA J ET AL: "Identification of 5-fluorouracil inducible target genes using cDNA microarray." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 44, July 2003 (2003-07), page 797, XP001182950 & 94TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; WASHINGTON, DC, USA; JULY 11-14, 2003 ISSN: 0197-016X abstract ----- -/--	1-20		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input type="checkbox"/> Patent family members are listed in annex.				
<b>* Special categories of cited documents:</b> <table border="0"> <tr> <td style="vertical-align: top;">           "A" document defining the general state of the art which is not considered to be of particular relevance            "E" earlier document but published on or after the international filing date            "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)            "O" document referring to an oral disclosure, use, exhibition or other means            "P" document published prior to the international filing date but later than the priority date claimed         </td> <td style="vertical-align: top;">           "I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention            "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone            "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art            "&amp;" document member of the same patent family         </td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family			
Date of the actual completion of the international search 17 January 2005		Date of mailing of the international search report 04.05.2005		
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3018		Authorized officer Gabriels, J		

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB2004/003342

C/(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MAXWELL PAMELA J ET AL: "Identification of 5-FU inducible genes in tumour cell lines by cDNA microarray" BRITISH JOURNAL OF CANCER, vol. 86, no. Supplement 1, June 2002 (2002-06), page S21, XP001202678 & BRITISH CANCER RESEARCH MEETING 2002; GLASGOW, UK; JUNE 30-JULY 03, 2002 ISSN: 0007-0920 abstract	1-20
A	----- LONGLEY DANIEL B ET AL: "5-fluorouracil: Mechanisms of action and clinical strategies." NATURE REVIEWS CANCER, vol. 3, no. 5, May 2003 (2003-05), pages 330-338, XP008039669 ISSN: 1474-175X the whole document	1-20
T	----- MAXWELL PAMELA J ET AL: "Identification of 5-fluorouracil-inducible target genes using cDNA microarray profiling." CANCER RESEARCH, vol. 63, no. 15, 1 August 2003 (2003-08-01), pages 4602-4606, XP002311056 ISSN: 0008-5472 the whole document -----	1-20